UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,564	10/18/2005	Alastair Magnaldo	434299-669	2050

46188 7590 03/16/2011
Nixon Peabody LLP
P.O. Box 60610
Palo Alto, CA 94306

EXAMINER	
KWAK, DEAN P	

ART UNIT	PAPER NUMBER
1773	

MAIL DATE	DELIVERY MODE
03/16/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,564	MAGNALDO ET AL.	
	Examiner	Art Unit	
	Dean Kwak	1773	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/07/2011 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in Graham **v.** John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-13, 16 & 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pawliszyn (US 4940333) and further in view of Fujiwara et al. (Liquid Core Optical Fiber Total Reflection Cell as a Colorimetric Detector for Flow Injection Analysis, Anal. Chem. 1985, 57, 1012-1016).

Regarding Claims 1 & 12, Pawliszyn teaches a method for analyzing a liquid sample (e.g., concentration gradient detection, see Abstract) by injecting the liquid sample in a reaction loop (e.g., sample chamber, Fig. 12 (90); see also C9/L43 & Fig. 9 (54), Fig. 5 (25)), comprising a transparent pipe (C5/L49), coupled with illumination means (e.g., probe light beam 93 generated by a laser 94 in Fig. 12, C11/L18; see also LED 66 coupled to optical fiber 67, C9/L58 & Fig. 9; LED 82 coupled to an optical fiber 79 in Fig. 10), comprising a light emitting diode (C2/L22), and detection means (e.g., optical fibers, C11/L59 & Fig. 12 (97); beam position detector, C9/L60 & Fig. 9 (68); light detector, C10/L29-32), comprising a diode array (e.g., photodiode detector, C10/L50; see also detector 103, sensors 104, 106 in Fig. 13 & C12/L25-55) aligned on the reaction loop (see Figs. 5, 6, 9, 10, 12 & 13), to record levels of light representative of the characteristics of the sample (e.g., concentration gradient, Abstract & C11/L54-63), said method comprising the following steps:

- filling the reaction loop (see the solvent and sample supplied under pressure by pumps, C9/L49-51) with a minimum volume of the sample (61) through a first input (60) of a T-shaped (57) branch and its output, said output being connected to said reaction loop (see Fig. 9),
- injecting at least one fixed volume of at least one reagent (e.g., solvent 59) into the reaction loop via a second input (58) of the T-shaped branch to obtain a mixture of the sample with the reagent(s), such that a concentration gradient (Abstract & C11/L54-63) is established in the reaction loop,
- illuminating the transparent pipe with the illumination means (C11/L13-21 & C11/L54-63),
- filtering the light transmitted through the transparent pipe (see the system using an optical filter 50, C9/L24-27),
- recording levels of light transmitted through said transparent pipe by the detection means after filtering, thereby revealing the characteristics of the sample (see C9/L8-27 & C12/L10-24), and
- calibrating the response (it is noted that calibrating steps is inherent in concentration gradient analysis (Abstract & C11/L54-63), since the sample must be base-lined & calibrated with the analyzer prior to obtaining concentration gradient curve),
- revealing the characteristics of the sample (e.g., concentration gradient, Abstract & C11/L54-63), and

- discharging the reagents located in the reaction loop (see tubing 62, 63 leads to waste, C9/L51-55).

Regarding Claims 1 & 12, Pawliszyn fails to teach the length of a transparent pipe or the flow rate. While Pawliszyn does not explicitly disclose the transparent pipe with a length between about 0.5 cm and about 10 cm or the flow rate of about 10 to about 1,000 μL/min, the change in the pipe length or the flow rate are not considered to confer patentability to the claims. Pawliszyn utilizes optical detection system to develop concentration gradient of specific chemical compounds (Abstract) where various changes may be made in adapting to different design requirements (C12/L65-68). It would have been obvious to one having ordinary skill in the art at the time the invention was made to adjust the pipe dimensions and the flow rate so that enough retention time required to mix the sample and therefore, accurate detection can be achieved. Therefore the pipe length and the flow rate are a variable that can be modified, among others, by varying the pipe used and changing the flow rate. For that reason, the pipe length and the flow rate would have been considered a result effective variable by one having ordinary skill in the art at the time the invention was made. As such, without showing unexpected results, the pipe length or the flow rate cannot be considered critical. Accordingly, one of ordinary skill in the art at the time the invention was made would have modified, by routine experimentation and optimization, the system of Pawliszyn to have a transparent pipe with a length between about 0.5 cm and about 10 cm and a flow rate of about 10 to about 1,000 μL/min (In re Boesch, 617 F.2d. 272, 205 USPQ 215 (CCPA 1980)), since it has been held that where the general conditions of

the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (In re Aller, 105 USPQ 223).

Regarding Claims 1 & 12, Pawliszyn fails to teach using a push-syringe or using a dye to detect at least one color change.

Fujiwara et al. teach a method for analyzing a liquid sample by injecting the liquid sample (Abstract) in a reaction loop (e.g., hollow fiber type long capillary cell (LCC), Abstract & Fig. 1), comprising a transparent pipe (e.g., optical fiber, P1012/right column/¶[2), coupled with illumination means (e.g., light source, Abstract), and detection means (e.g., automated detection system, P1013/right column) to record levels of light representative of the characteristics of the sample (e.g., color development, Experimental Section), said method comprising the following steps:

- filling the reaction loop with a minimum volume of the sample (P1015/left column/last paragraph) through a first input of a T-shaped branch (see Fig. 4 where the sample 1 flows into a Y-shaped branch) and its output, said output being connected to said reaction loop (see Fig. 4),
- injecting at least one fixed volume of at least one reagent containing a dye (e.g., solution for color development 15, Fig. 4) into the reaction loop via a second input of the T-shaped branch (Fig. 4) and its output in using a push-syringe (P1015/left column/last paragraph) to obtain a mixture of the sample with the reagent(s), such that a colorimetric detection is established in the reaction loop establishing at least one color change point,

- illuminating the transparent pipe with the illumination means (P1013/Detection System for Iodine Absorption),
- filtering the light transmitted through the transparent pipe (e.g., band-pass filter, Fig. 3 & P1013/Detection System for Iodine Absorption), so that the position of the at least one color change point is determined (see Figs. 7 & 8),
- recording levels of light transmitted through said transparent pipe by the detection means after filtering (see Figs. 7 & 8),
- calibrating the response (it is noted that calibrating steps is inherent in flow injection analysis, since the sample must be base-lined & calibrated with the analyzer prior to obtaining colorimetric detection curve),
- revealing the characteristics of the sample (see Figs. 7 & 8), and
- discharging the reagents located in the reaction loop (e.g., drain, Fig. 4).

Regarding using a syringe, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Pawliszyn to use a syringe, as taught by Fujiwara et al., since syringe is notoriously well known in the flow injection analysis, readily available & economical. In addition, it would have been obvious to use a microliter syringes, as taught by Fujiwara et al. (P1013/Detection System for Iodine Absorption), to accurately control flow rates in micro volumes.

Regarding using a dye, it would have been obvious to one of ordinary skill in the art to modify the system of Pawliszyn with a dye solution, as taught by Fujiwara et al., to improve detection sensitivity of colorimetry, see Fujiwara et al./P1012.

Regarding Claims 2-7, 9-11, 13 & 17, modified Pawliszyn further teach the method, wherein:

- a concentration gradient is detected in the reaction loop (see Abstract);
- the reaction loop is a transparent capillary channel (e.g., capillary tube, C9/L41 & Fig. 9 (51); also see the tube having transparent sides, C5/L49);
- the discharge of the reagents located in the reaction loop is performed by means of the remaining sample (C9/L51-55);
- the discharge of the reagents located in the reaction loop is performed by means of the next sample (C6/L33-35);
- the sample flux is not interrupted, which allows continuous analysis (C6/L35-46);
- fixed volumes of reagents are successively injected during predefined time intervals (C6/L33-46);
- linear detection is performed along the reaction loop (see the optical fibers Fig. 12 (97), Fig. 10 (79, 83) placed linearly along the "reaction loop" to obtain concentration gradient curve as shown in Fig. 7);
- a point detection (e.g., optical fibers, Fig. 12 (97), C11/L59; Fig. 10 (79 & 83), C10/L26 & 30) is achieved in a location of the reaction loop;
- the diode array comprises a point sensor (C5/L54);
- the transparent pipe is a transparent capillary or a microfluidic channel (e.g., capillary tube, C9/L41 & Fig. 9 (51); also see the tube having transparent sides, C5/L49); and

- a microvalve (e.g. valve, Fig. 9 (57)) positioned upstream from the point of introduction of the sample into the reaction loop.

Regarding Claim 8, Pawliszyn fails to teach the flow rate. While Pawliszyn does not explicitly disclose the flow rate of about 10 to about 1,000 μL/min, the flow rate is not considered to confer patentability to the claims. Pawliszyn utilizes optical detection system to develop concentration gradient of specific chemical compounds (Abstract) where various changes may be made in adapting to different design requirements (C12/L65-68). It would have been obvious to one having ordinary skill in the art at the time the invention was made to adjust the flow rate so that enough retention time required to mix the sample and therefore, accurate detection can be achieved. Therefore the flow rate is a variable that can be modified, among others, by varying the flow rate. For that reason, the flow rate would have been considered a result effective variable by one having ordinary skill in the art at the time the invention was made. As such, without showing unexpected results, the flow rate cannot be considered critical. Accordingly, one of ordinary skill in the art at the time the invention was made would have modified, by routine experimentation and optimization, the system of Pawliszyn to have a flow rate of about 10 to about 1,000 μL/min (In re Boesch, 617 F.2d. 272, 205 USPQ 215 (CCPA 1980)), since it has been held that where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (In re Aller, 105 USPQ 223).

Regarding Claim 11, although Pawliszyn teaches the optical fibers are glued (C5/L54), it is noted that gluing can be unglued to relocate the detector to another position. One of ordinary skill in the art would have desired a means for fixing the fibers during use, yet still allow for mobility to move the fibers to another location at a later date. In this instance, the claim only requires the ability of the component to be movable, but does not limit the manner in which is it movable. Absent any particular claim language to a use of a structure to move the point sensor, the language of "configured to be movable" is read as merely the ability to do so, thereby an act of gluing and ungluing encompasses a configured ability to meet the limitation.

Regarding Claim 16, Pawliszyn fails to disclose a peristaltic pump.

Fujiwara et al. further teach the flow injection analysis system comprising a peristaltic pump allowing introduction of the sample (P1014/Automatic Detection System for Iodine Ion & Fig. 4 (2)).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a peristaltic pump, as taught by Fujiwara et al., since a peristaltic pump allows liquid to flow at a constant flow rate as well as ability to be operated under automated system, see Experimental Section.

Response to Arguments

6. Applicant's arguments filed 02/07/2011 have been fully considered but they are not persuasive.

7. In response to applicants' argument regarding Pawliszyn fails to teach a diode array, Examiner disagrees. Pawliszyn teaches optical fibers (C11/L59 & Fig. 12 (97)), beam detector (C9/L60 & Fig. 9 (68)), light detector (C10/L29-32), comprising a photodiode detector (C10/L50) and a diode array (detector 103, sensors 104, 106 Fig. 13 & C12/L25-55). The photodiode D3 that applicants' are relying on is a part of example given by the examiner. As set forth above, the reference teaches a plurality of detectors arranged around the sample chamber for detecting a concentration gradient by measuring the amount of deflection of a probe light beam caused by the gradient.

8. In response to applicants' argument regarding the arrangement of the diode array, i.e., aligned on the reaction loop, the claim only specified the diodes are aligned (i.e., arranged in a linear manner). Exemplary of this arrangement is shown in Figs. 6 & 13, where sensors/detectors are aligned on the sample chamber. In addition, claim 1 is not specific as to alignment steps required for analyzing a liquid sample.

9. In response to applicants' argument regarding Pawliszyn device is impossible to determine the position of the at least one color change point, Examiner disagrees. It is noted that Pawliszyn measures the intensity of light, which the intensity (brightness of the light) inherently corresponds to a range of wavelengths (i.e., frequencies, such as color). The fact that Pawliszyn teaches detecting concentration gradient by use of light beam & detectors and that the intensity of light corresponds to the gradient, it reads on the limitation. In addition, Fujiwara et al. was relied on for the teachings of analyzing a liquid sample using color development (dye), see above.

Conclusion

10. This is a RCE of applicant's earlier Application No. 10/553564 All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dean Kwak whose telephone number is 571-270-7072. The examiner can normally be reached on M-TH, 5:30 am - 4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

07 March 2011

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1773

/D. K./
Examiner, Art Unit 1773